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Department:
Health
REPUBLIC OF SOUTH AFRICA



**South African National Essential Medicines List
Adult Hospital Level Medication Review Process
Economic evaluation and budget impact analysis for costing model – summary report
Component: Gynaecology**

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Affiliation/ conflicts of interest: Health Economics and Epidemiology Research Office, University of Witwatersrand; no conflicts of interest declared.

MEDICINE: Levonorgestrel intrauterine system (ATC: G03AC03)

BACKGROUND

Abnormal Uterine Bleeding (AUB) is defined by the FIGO PALM COEIN classification as heavy menstrual bleeding (HMB) that lasts more than 8 days or results in greater than 80ml blood loss per cycle. AUB has a significant negative impact on quality of life resulting from excessive, prolonged blood loss, particularly when combined with menstrual pain. There are a number of treatment options available for AUB including medical management such as non-steroidal anti-inflammatories, tranexamic acid, hormonal therapy (e.g. oral contraceptives), levonorgestrel intrauterine system (LNG-IUS) or surgery (hysterectomy or endometrial ablation).

Increasingly evidence has shown that the LNG-IUS is as effective, if not more effective, in treating AUB compared to medical management or surgery and in recent years, the adoption of the LNG-IUS as a first-line treatment for AUB in Europe and the US has been widespread. However, its availability and accessibility has been limited in developing countries, largely due to concerns around price and affordability. The aim of this analysis was to determine the cost-effectiveness and budget impact of the LNG-IUS in a public sector setting in South Africa in order to inform whether the LNG-IUS should be included on the Essential Medicines List for the treatment of heavy menstrual bleeding.

MODEL DESIGN AND INPUTS

A decision tree analysis was developed for two populations; women who were in their fertile years (either requiring contraception or wanting to fall pregnant) and older women who were pre- or peri-menopausal using current the standard of care as a comparator. The LNG-IUS was introduced into the model as third line therapy (i.e. after failure of medical management). A time horizon of 5 years was used.

The clinical inputs to the model were based on probabilities of treatment success (well) or treatment failure (unwell) as well as the quality of life experience by patients in each treatment arm (as determined by utilities). Since there are no data available in South Africa on the probabilities or utilities for treatment options in AUB, published data were used to inform the inputs.

Costs of medicines, the LNG-IUS, clinic visits, surgery (hysterectomy) were obtained from local data and adjusted to a baseline of 2018 prices.

COST-EFFECTIVENESS ANALYSIS

The results of the cost-effectiveness analysis show that for the 5-year time horizon, the LNG-IUS had improved clinical benefits and fewer costs, thereby making it dominant over the medical management option. For the 1-year time horizon, the incremental benefits were lower than the 5 years; but the total costs were slightly higher compared to medical management resulting in an ICER of R6 442/QALY and R19 235/QALY for the 15-44 year cohort and the 45-59 year cohort, respectively. This is in line with other published cost-effectiveness analyses where the LNG-IUS has been shown to be dominant compared to medical and surgical management (Ganz et al, 2013; Calaf et al, 2015; Spencer et al, 2017).

COC/PRG	QALYs	Incremental QALYs	Costs	Incremental Costs	ICER (R/QALY)
LNG-IUS	3.79		6 326.61		
No LNG-IUS	3.68	0.11	8 008.62	- 1 682.01	Dominant
OC+MPA	QALYs		Costs		ICER (R/QALY)
LNG-IUS	3.79		11 995.13		
No LNG-IUS	3.68	0.11	14 813.20	- 2 818.07	Dominant

Table 1. Costs and QALYs for a 5-year time horizon

COC/PRG	QALYs	Incremental QALYs	Costs	Incremental Costs	ICER (R/QALY)
LNG-IUS	0.82		1 878.67		-
No LNG-IUS	0.81	0.01	1 823.65	55.02	6 443.26
OC+MPA	QALYs		Costs		ICER (R/QALY)
LNG-IUS	0.82		3 346.64		-
No LNG-IUS	0.81	0.01	3 205.84	140.80	19 235.43

Table 2. Costs and QALYs for a 1-year time horizon

Sensitivity analysis showed that in most instances the model remained dominant (ie LNG-IUS had lower costs and better clinical outcomes) regardless of changes in the variable inputs. The model was most sensitive to the probability of patients no longer receiving treatment following treatment failure with first and second line medical management or LNG-IUS. This was the only parameter that shifted the ICERs from being dominant to an increased cost for the LNG-IUS with an increased clinical benefit. However, even with a probability of 80% of patients no longer receive any treatment; the ICERs were still below R10 000/QALY

BUDGET IMPACT ANALYSIS

The Budget Impact Analysis shows that the total costs of treating AUB run into hundreds of millions of rands per annum assuming only women eligible in the public sector with a probability of 37.4% of AUB, where only 38% would seek treatment and of those patients, only 20% would receive the LNG-IUS. The incremental difference in cost in patients aged 15-44 years (COC/PRG) is around R30 million per year (2018). However, for the patients ages 45-59 and 45-54 years a savings of R39 million and R28 million is achieved respectively with the use of the LNG-IUS. Furthermore, if the model is run over 5 years for that same cohort (ie receive LNG-IUS in Year 1) then the model shows that the LNG-IUS is cost saving in the longer term. The total budget impact is less in the 45-54 years population due to a reduction in numbers of people in that cohort.

The average cost increment per patient is just over R87 in Year 1 in patients who have had the LNG-IUS placed, however for patients who are peri-menopausal, a savings of around R462 is achieved in the first year. This is due to the higher cost of hormone treatment (R168 per month) contributing significantly to the total costs in this patient cohort.

COC/PRG	Costs (Yr 1)	Difference	Costs (Yr 1-5)	Difference
LNG-IUS	815 598 885		2 037 953 566	
No LNG-IUS	785 393 171	30 205 715	4 171 417 216	-2 133 463 651
OC+MPA (45-59 yrs)				
LNG-IUS	281 033 742		789 950 877	
No LNG-IUS	320 714 819	-39 681 078	1 730 457 578	-940 506 701
OC+MPA (45-54 yrs)				
LNG-IUS	199 831 298		561 700 912	
No LNG-IUS	228 046 847	-28 215 549	1 230 455 752	-668 754 839

Table 3. Budget impact on total costs for a 5-year time horizon

COC/PRG	Costs (Yr 1) per pt	Difference	Costs (Yr 1-5) per pt	Difference
LNG-IUS	2 351		5 875	
No LNG-IUS	2 264	87	12 025	-6 150
OC+MPA (45-59 yrs)				
LNG-IUS	3 272		9 196	
No LNG-IUS	3 734	-462	20 145	-10 949
OC+MPA (45-54 yrs)				
LNG-IUS	3 272		9 196	
No LNG-IUS	3 734	-462	20 145	-10 949

Table 4. Budget impact on costs per patient for a 5-year time horizon

CONCLUSION AND RECOMMENDATIONS

The introduction of the LNG-IUS as a third line treatment for heavy menstrual bleeding in South Africa is shown to be dominant, i.e. costs less and has a better clinical benefit in both the younger and older cohorts. This is largely due to the ongoing pharmacotherapy treatment costs of patients year on year compared to the once-off cost of the LNG-IUS in the first year. Variations in input parameters in the sensitivity analysis fail to shift the dominance with the exception of increasing the probability of no treatment to 59%.

The budget impact analysis shows a substantial level of costs for the treatment of AUB. In the first year of treatment, the LNG-IUS cohort has higher costs in the 15-44 year age group compared to those on medical management (ie No LNG-IUS). In the older patient cohort (45-59 years) the budget impact shows a savings in the LNG-IUS group. Over a 5-year time period it is proven to be cost-saving for both cohorts (age 15-44 and age 45-59).

This evaluation has been based on clinical inputs from international studies as there is no local data to draw upon. It is recommended that a costing analysis be conducted to determine how much treatment of AUB actually costs in South Africa in the public sector as well as a survey of numbers of patients requiring treatment and their treatment preferences.

NEMLC MEETING OF 27 SEPTEMBER 2018 & 21 FEBRUARY 2019:

- NEMLC recommended that LNG-IUS be included on the Tertiary & Quaternary EML for abnormal uterine bleeding, where there has been treatment failure – prescribed and administered by gynaecologists. (However, consumption, uptake and budgetary impact to be monitored to inform whether LNG-IUS for AUB should be accessed universally at secondary level of care, going forward).

Rationale: LNG-IUS for abnormal uterine bleeding has been shown to be cost-effective, but is not affordable for inclusion to the secondary level EML. Tertiary level of care would provide a more controlled environment to monitor the use of LNG-IUS. Furthermore, it would be the discretion of the Tertiary facility/Provincial Pharmaceuticals and Therapeutics Committee to enable access of this intervention at lower levels of care.

Level of Evidence: I Systematic review, Expert opinion

Minutes of the NEMLC meetings of 27 September 2018 & 21 February 2019

Other reference documents:

National Department of Health: Affordable Medicines, EDP-Adult Hospital level. Medicine Review: LNG-IUS for abnormal uterine bleeding/menorrhagia/heavy menstrual bleeding, June 2015. <http://www.health.gov.za/>

National Department of Health: Affordable Medicines, EDP-Adult Hospital level. Health Economics and Budget Impact Analysis: Levonorgestrel intrauterine system (LNG-IUS) for abnormal uterine bleeding/menorrhagia/heavy menstrual bleeding, December 2018. <http://www.health.gov.za/>

National Department of Health, Essential Drugs Programme: Tertiary and Quaternary Essential Medicines List, December 2018. <http://www.health.gov.za/>